UNIVERSITY OF CAMBRIDGE

Foetal testosterone and autistic traits

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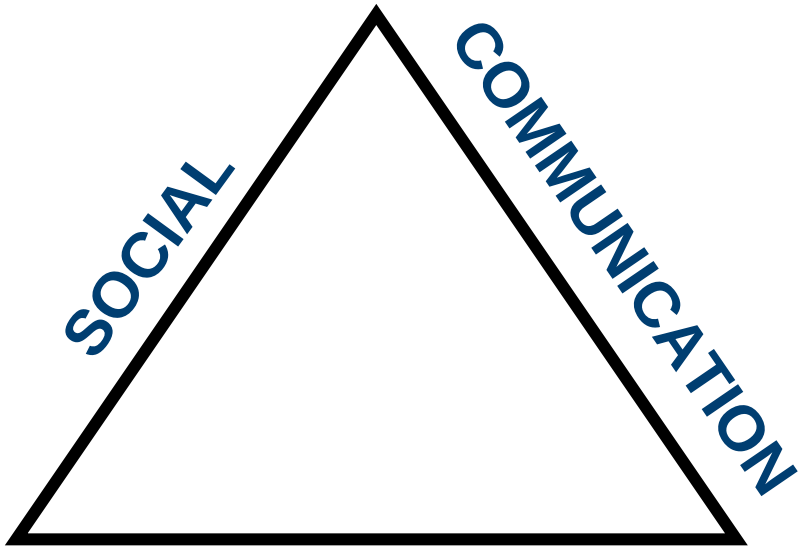
Characteristics of Autism Spectrum Conditions

Spectrum of Conditions with:

- Impairments in:
  - Social Interaction
  - Communication
- Restricted Interests
- Repetitive Behaviours
- Affect 1% of the population



It has been suggested that these characteristics may be linked sex-typical behaviours in the wider population

Autism and ‘Maleness’

- Classic autism 4 males : 1 female (Chakrabarti & Fombonne, 2005)
- Asperger Syndrome >10 males : 1 female (Gillberg et al., 2006)

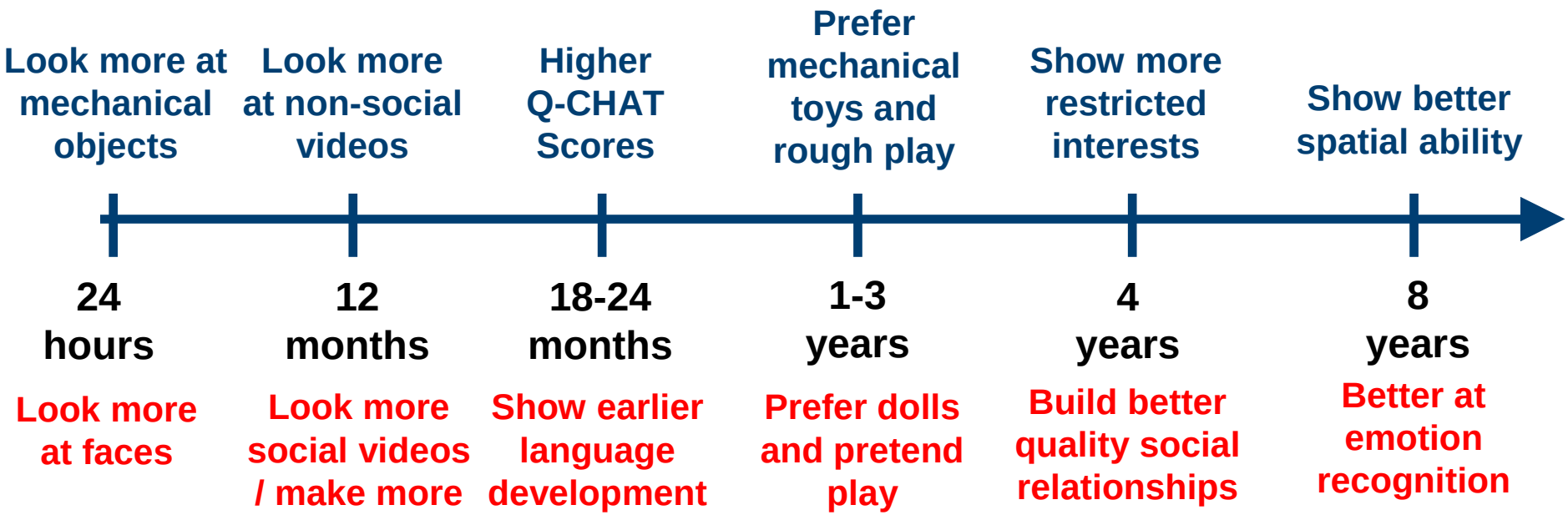
“The autistic personality is an extreme variant of male intelligence…

In the autistic individual the male pattern is exaggerated to the extreme”

Hans Asperger, 1944

What is ‘Maleness’ ?

BOYS

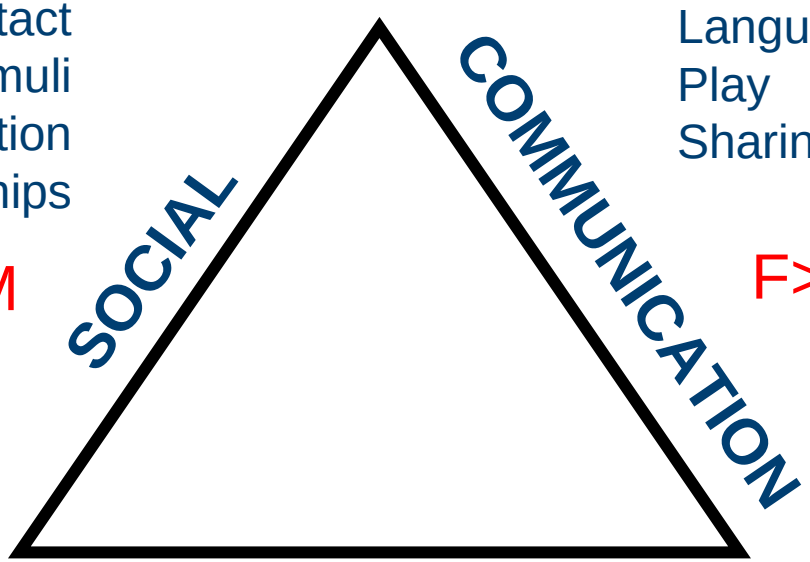


GIRLS

Characteristics

Eye contact
Social Stimuli
Face/Emotion recognition
Friendships

F>M



Language
Play
Sharing / Reciprocation

F>M

Narrow interests / Repetitive Behaviour

M>F

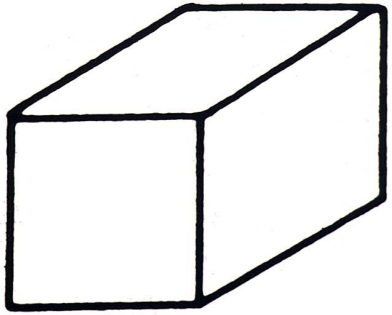
Early Development

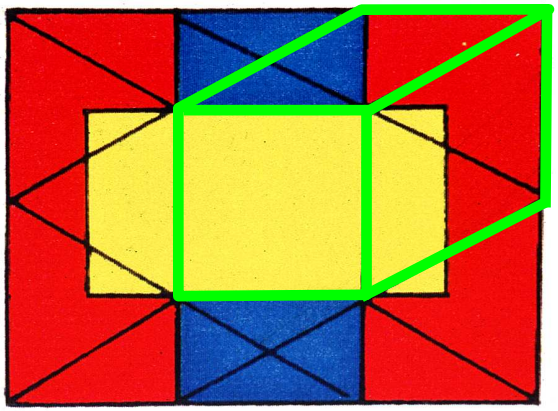
- 1-Year Well-Baby Check-Up
- 14-24 months
  - Toddlers with ASC look longer at geometric patterns
  - TD toddlers look longer at social images

(Pierce et al., 2010)

Sex Differences in Behaviour

- Areas of spatial ability have shown an advantage for males
  - Physical Prediction Questionnaire
    (Lawson et al., 2004)
  - Embedded Figures
    (Shah & Frith, 1983; Joliffe et al., 1997)





- Boys are more interested in moving cars and mechanical toys
  - Also observed in nonhuman primates

Primate Toy Choice

Alexander & Hines, 2002

Empathising and Systemising

- In order to consider trends across different behaviours, we can consider these skills as being part of two behavioural dimensions:
- Empathising
  - ***Drive to identify another person's emotions and thoughts, and to respond to these appropriately***
  - e.g. emotional recognition, communication
- Systemising
  - ***Drive to analyse, explore and construct a system***
  - e.g. identifying shapes, mechanisms and patterns

Empathy Quotient (EQ)

- Empathy Quotient is a questionnaire developed for both adults (EQ) and Children (EQ-C)

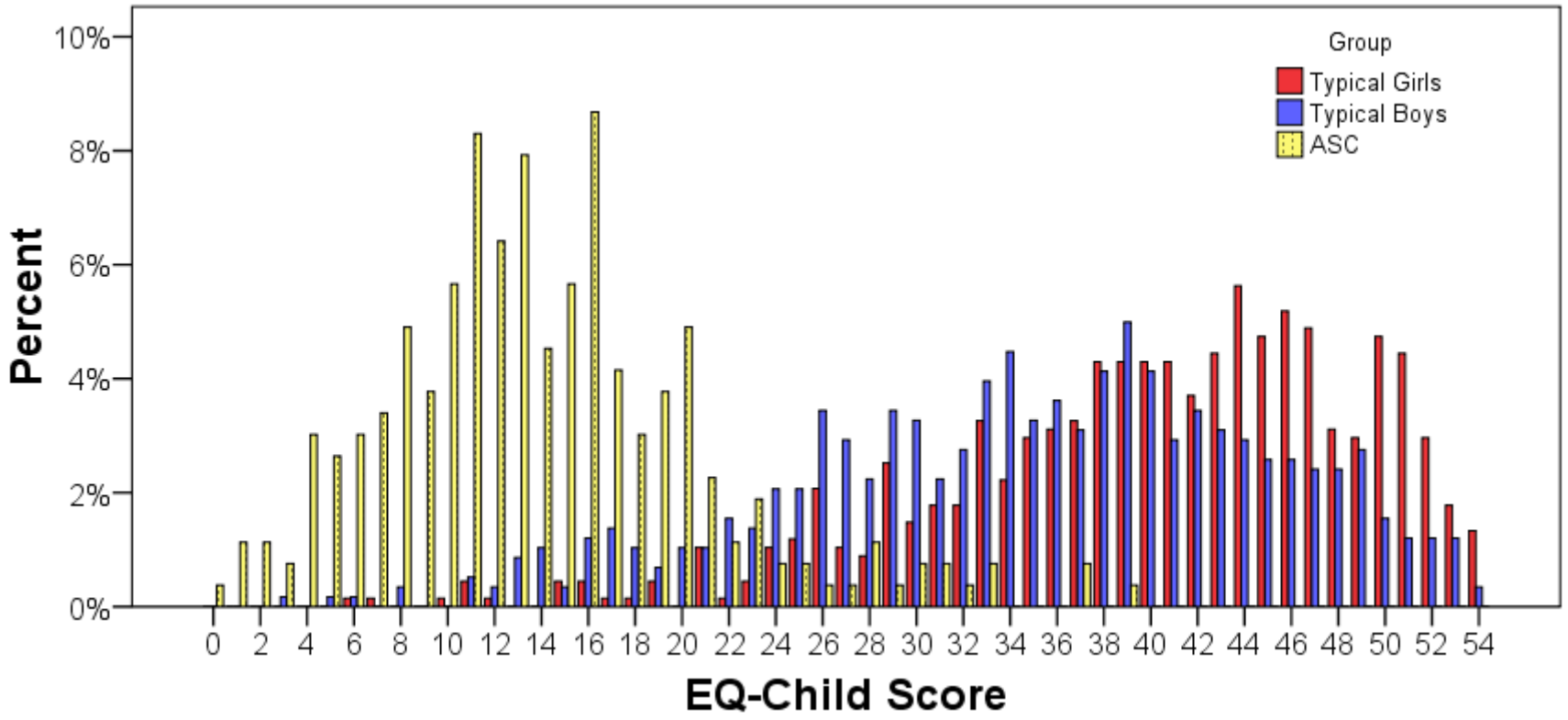
  - I really enjoy caring for people
  - I often find it difficult to judge if something is rude or polite

  - My child likes to look after other people.
  - My child is often rude or impolite without realising it

The Child Empathy Quotient (EQ-C)

- 265 children with ASC, 1256 with no diagnosis
- 4 to 11 years old (M=7.90, SD=1.77)

JADD, 2009



Systemising Quotient (EQ)

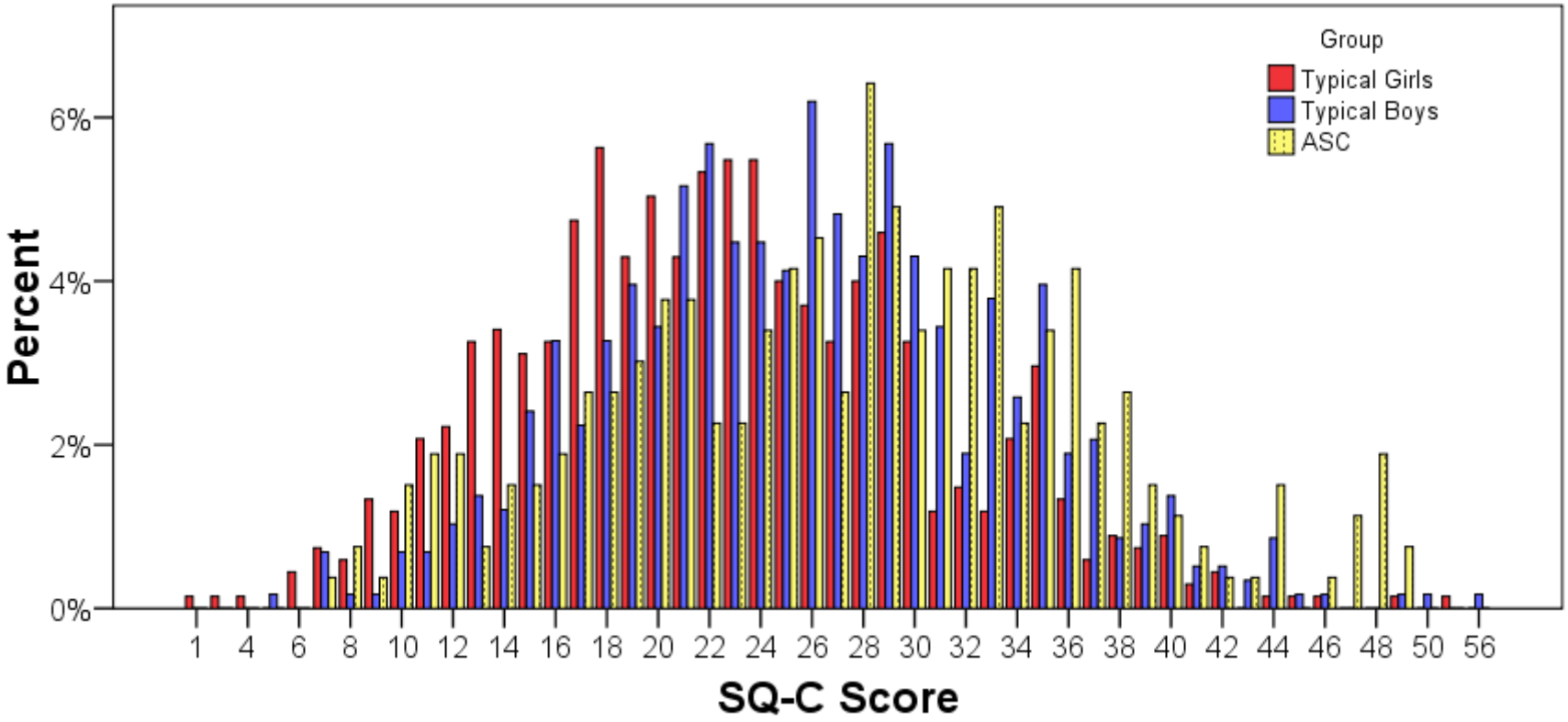
- Systemising Quotient is also developed for both adults (SQ) and Children (SQ-C)

- When I listen to a piece of music, I always notice the way it's structured
- In maths, I am intrigued by the rules and patterns governing numbers
- My child enjoys arranging things precisely (e.g. flowers, books, music collections)
- My child gets annoyed when things aren't done on time

The Child Systemising Quotient (SQ-C)

- 265 children with ASC, 1256 with no diagnosis
- 4 to 11 years old (M=7.90, SD=1.77)

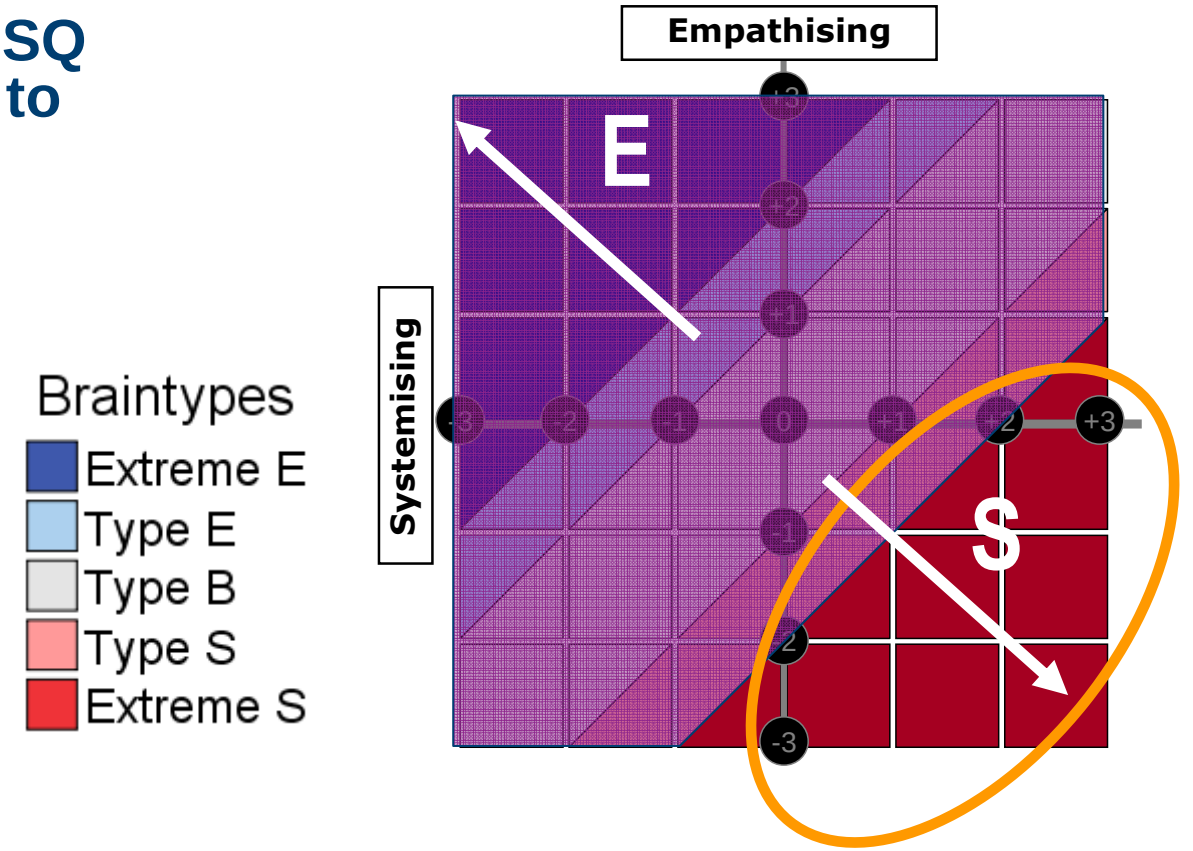
JADD, 2009



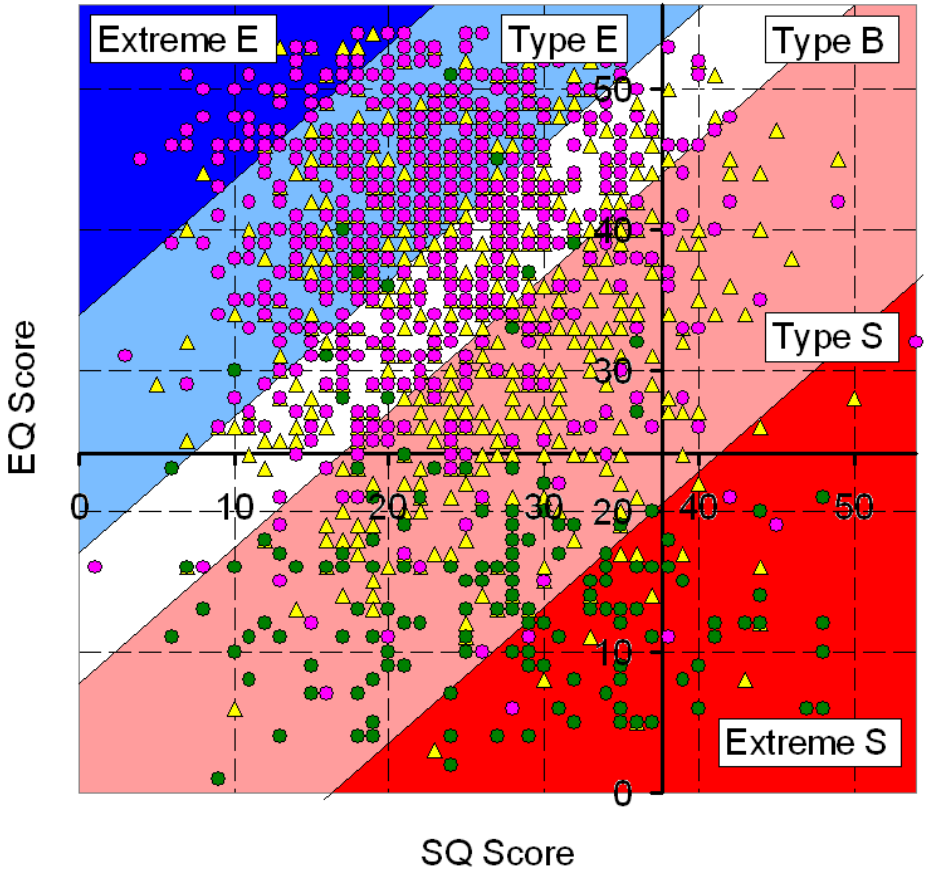
Empathising and Systemising

Cognitive ‘Brain types’

Normalised EQ and SQ scores can be used to define ‘brain types’



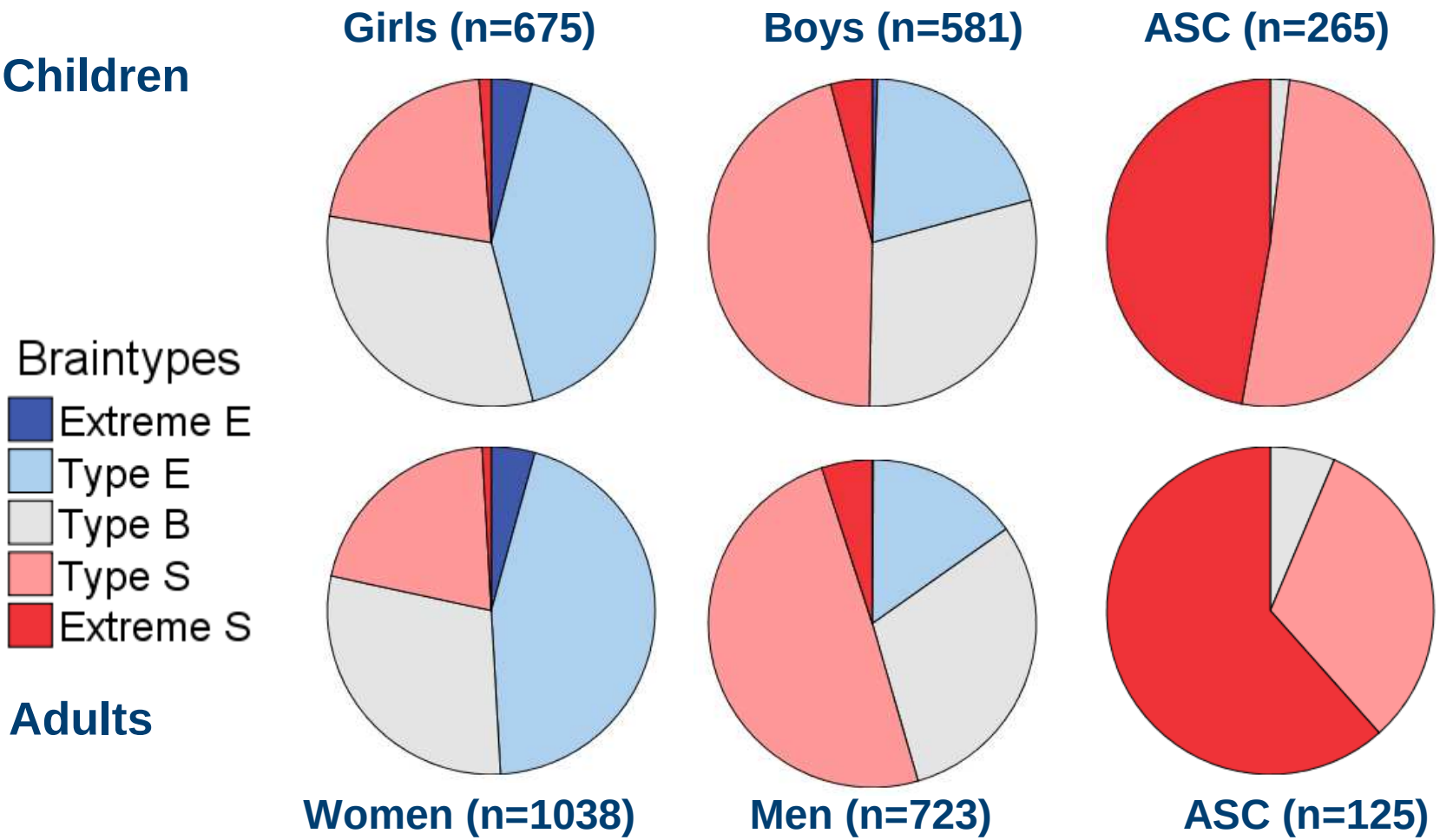
Child Brain types



Brain types	Girls n=675	Boys n=581	ASC n=265
Extreme E	4.0	0.5	0
Type E	41.9	20.3	0
Type B	31.7	29.5	1.9
Type S	21.2	45.6	50.9
Extreme S	1.2	4.1	47.2

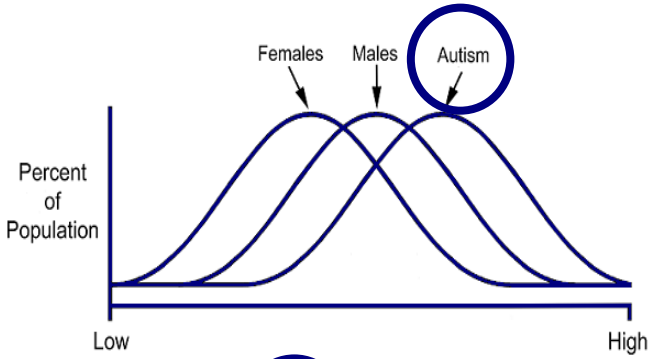
JADD, 2009

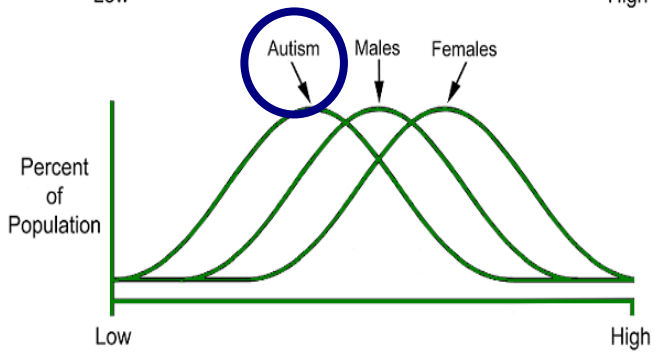
Brain type Proportions of Children and Adults



Empathising and Systemising

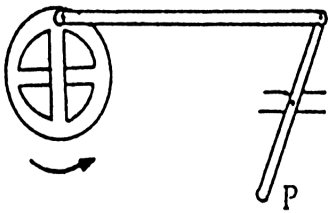
Systemising





Empathising

Physical Prediction Questionnaire
(Lawson et al., 2004)



If the wheel rotates as shown, P will
(a) move to the right and stop
(b) move to the left and stop
(c) move to and fro
(d) none of these

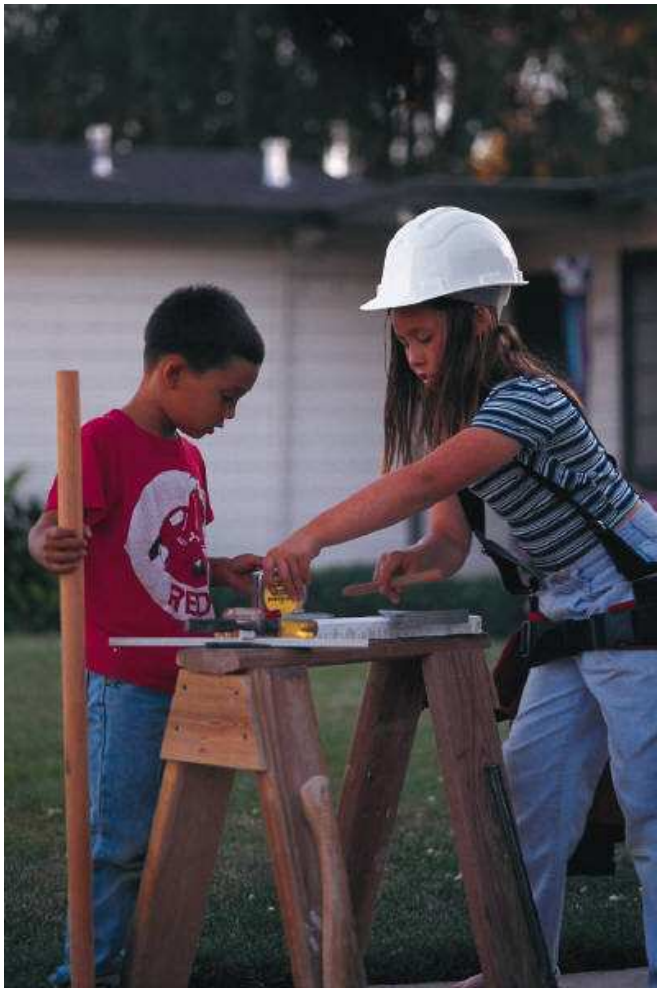
Eyes Test
(Baron-Cohen et al., 2001)

sarcastic **stern**

suspicious **dispirited**

What causes sex differences in behaviour?

- Possible causes include:
  - Parenting
  - Siblings
  - Education
  - Culture
  - Genes
  - Exposure to Hormones



Are sex differences linked to hormones?

- Hormones are used throughout the animal world to initiate and to regulate:
  - Physical development
  - Behavioural development
- Androgens (such as testosterone) have been shown to be particularly important for ‘male’ development
  - Testosterone injections during pregnancy masculinise behaviour in non-human mammals
  - Individuals with Androgen Insensitivity (AIS) develop as females

Testosterone in non-human mammals

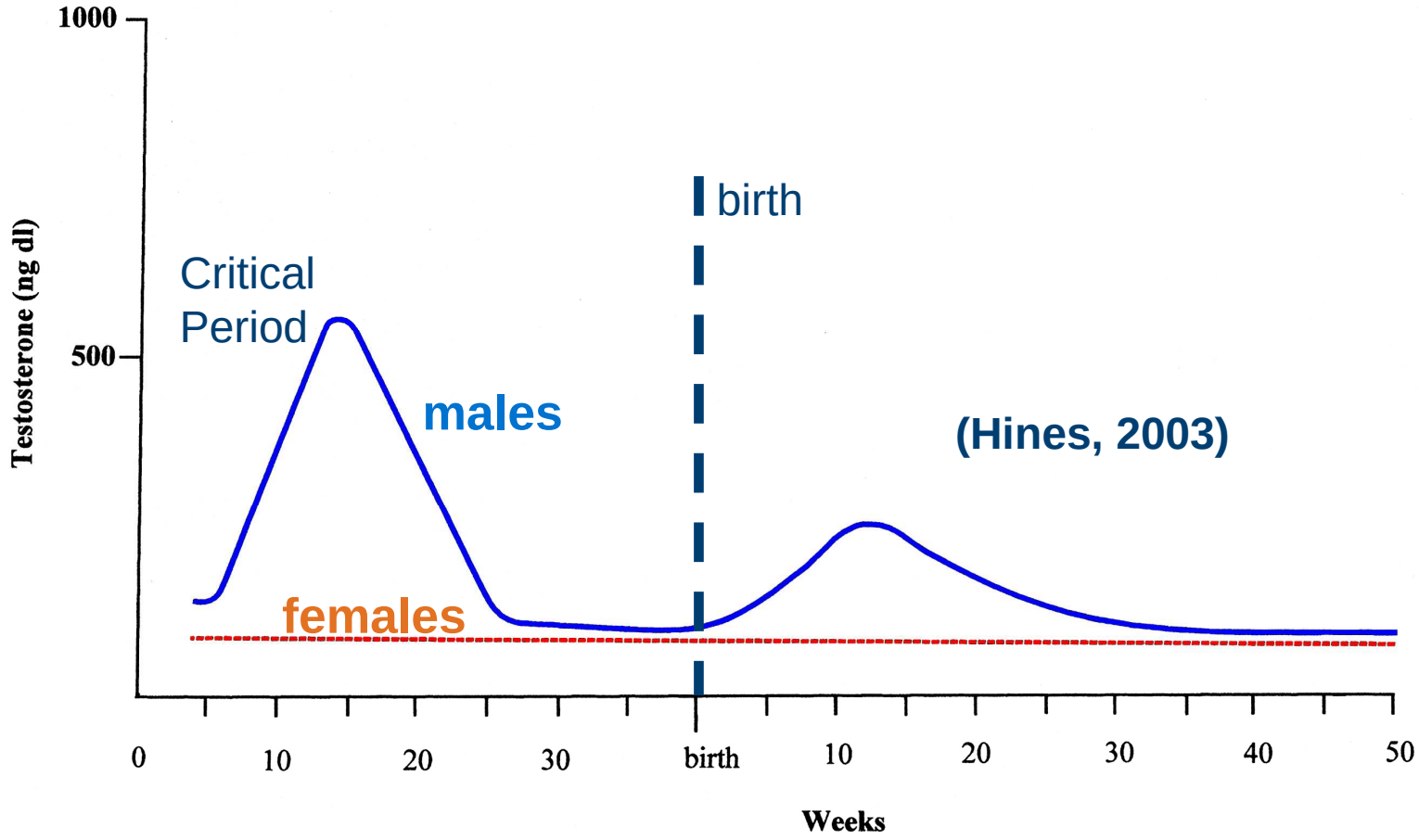
- Hormone manipulation affects:
  - Sexual development (Jost, 1947, 1953)
  - Brain development (Arnold & Gorski, 1984; Breedlove, 1994; MacLusky & Naftolin, 1981; Phoenix, 1959)
  - Sex-typical play (Alexander & Hines, 2002; Goy et al., 1988)
  - Spatial Ability (Williams & Meck, 1990, 1991)

Organisational vs Activational Effects

- Hormone effects are usually classified as:
  - Organisational (permanent, early in development)
    - occur during a sensitive (or critical) period
    - consistent with the development of ASC
  - Activational (transient, superimposed on the early organisational effects)
    - e.g. Puberty

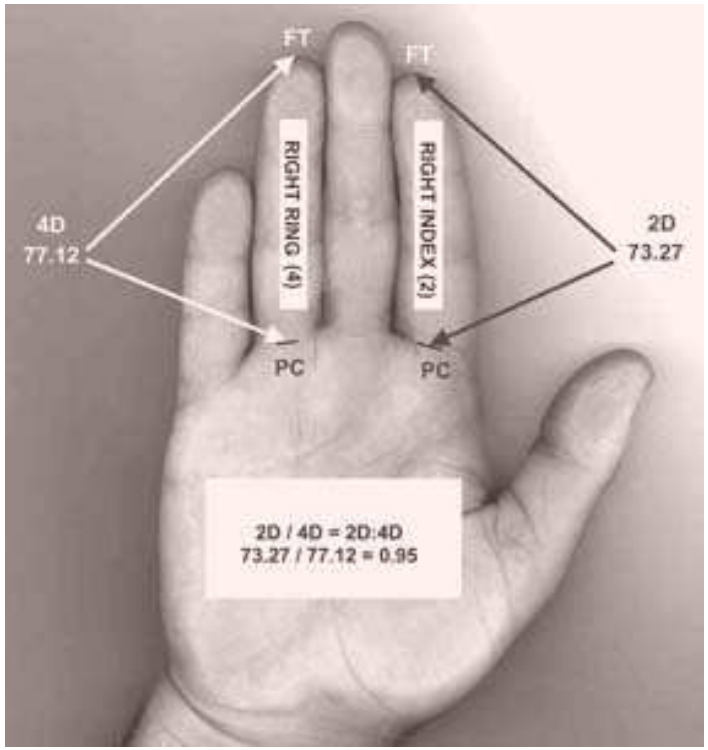
Foetal Testosterone (fT)

- Surges in Testosterone levels



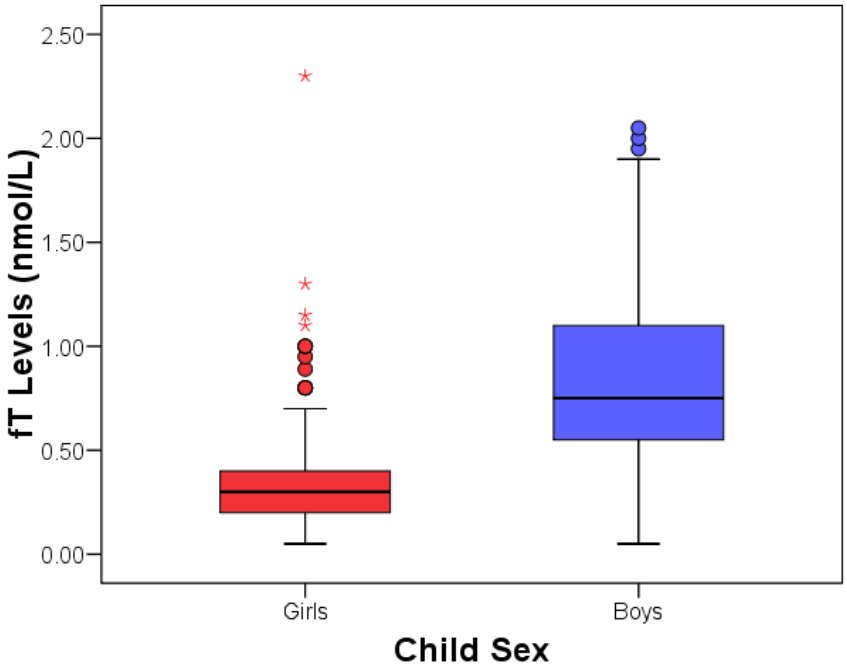
Prenatal hormones in humans

- Direct Manipulation not used
- Studies in clinical populations
  - Androgen Insensitivity Syndrome (AIS)
  - Congenital Adrenal Hyperplasia (CAH)
- Studies using proxy measures
  - Digit ratio
  - Maternal blood
- Studies using Amniocentesis



Sampling Amniotic Fluid (Amniocentesis)

- Advantages
  - Timing
  - Performed during 14-20 weeks of gestation
  - The foetus seems to be the origin of androgens

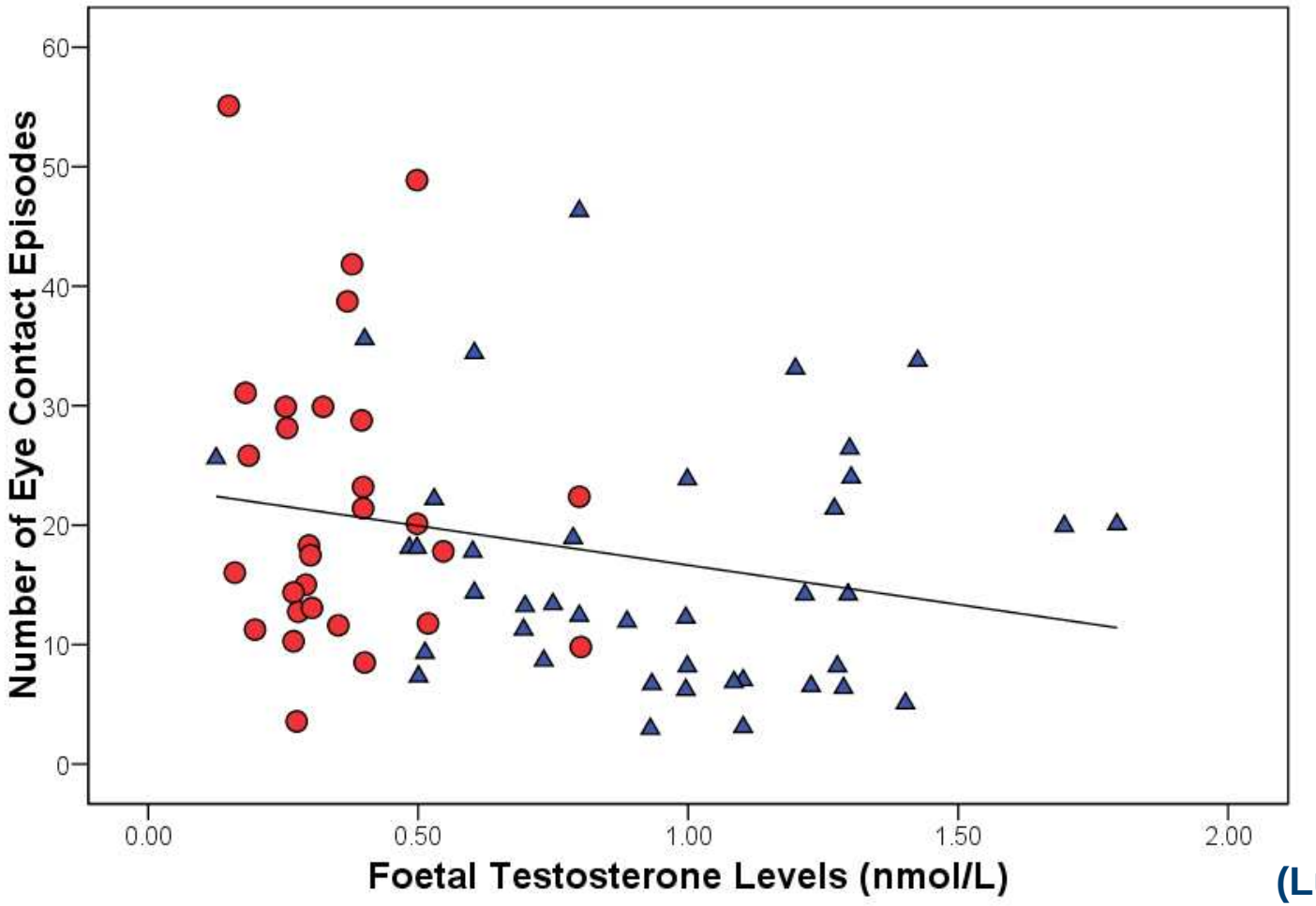


- Disadvantages
  - Invasive and risky
  - Cannot perform the procedure for research alone

The Cambridge Child Development Project

- Mothers all had amniocentesis
- Predictor variables
  - fT levels
  - Gestational age at amniocentesis
  - Parental age
  - Level of education obtained by parents
  - Number of siblings

fT and Eye Contact (12 months of age)

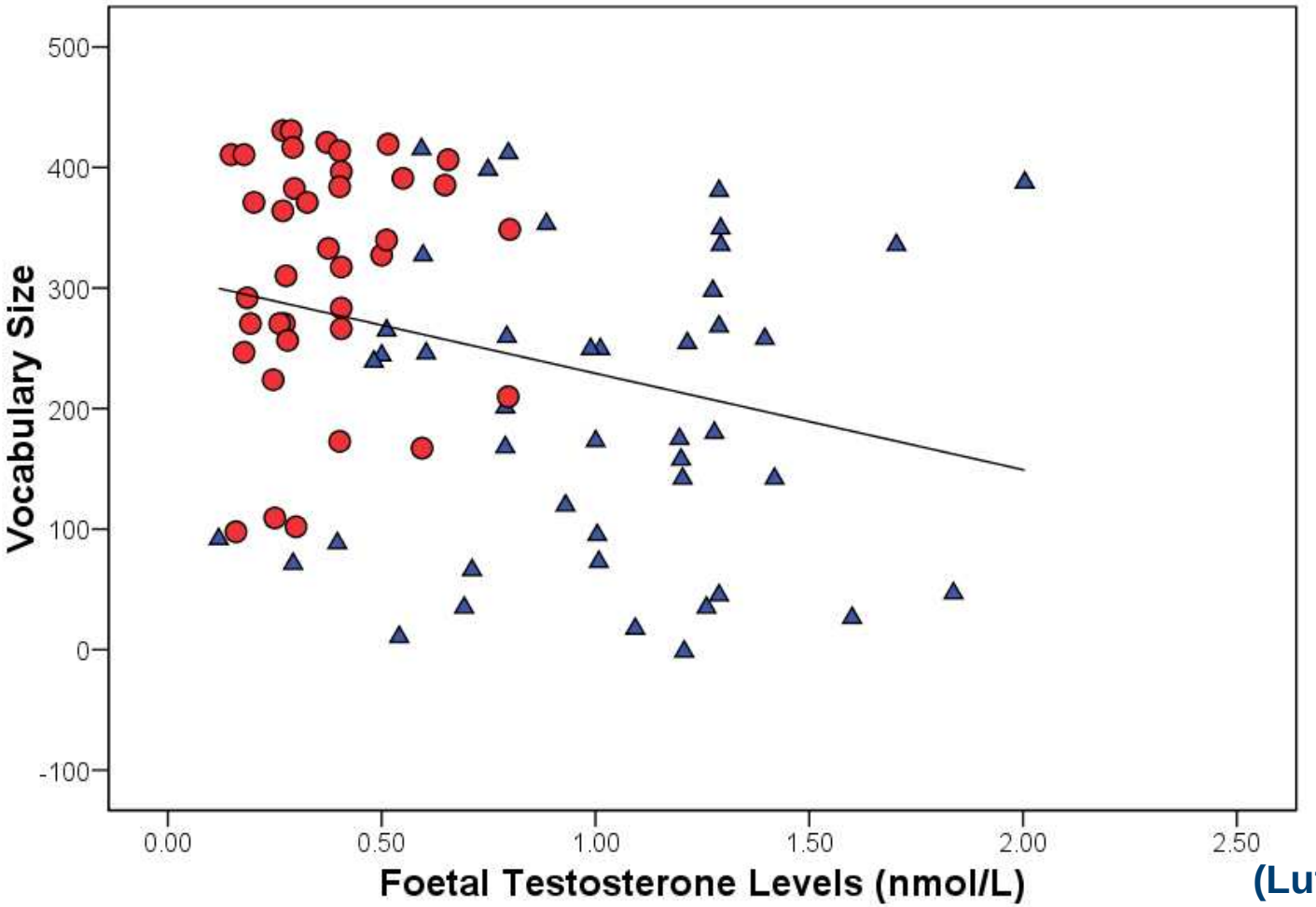


boys n=41	16.1 (10.0)
girls n=29	22.0 (12.1)

$r = -0.30$, $p < 0.01$

(Lutchmaya et al., 2002)

fT and Vocabulary Size



boys n=47	41.8 (50.1)
girls n=40	86.8 (83.2)

$r = -0.20$, $p < 0.01$

(Lutchmaya et al., 2002)

fT, Social Relationships and Restricted Interests

- Children's Communication Checklist

- Quality of Social Relationships
  - e.g. is s/he popular with other children
- Those with lower fT levels showed better quality of social relationships

boys n=35	32.38 (1.6)
girls n=23	33.0 (1.0)

- Restricted Interests
  - e.g. has one or more overriding specific interests (e.g., computers, dinosaurs) and will prefer doing activities involving this to anything else
- Those with higher fT levels had more restricted interests

boys n=35	30.7 (2.3)
girls n=23	32.1 (1.6)

(Knickmeyer et al., 2005)

Play Behaviour

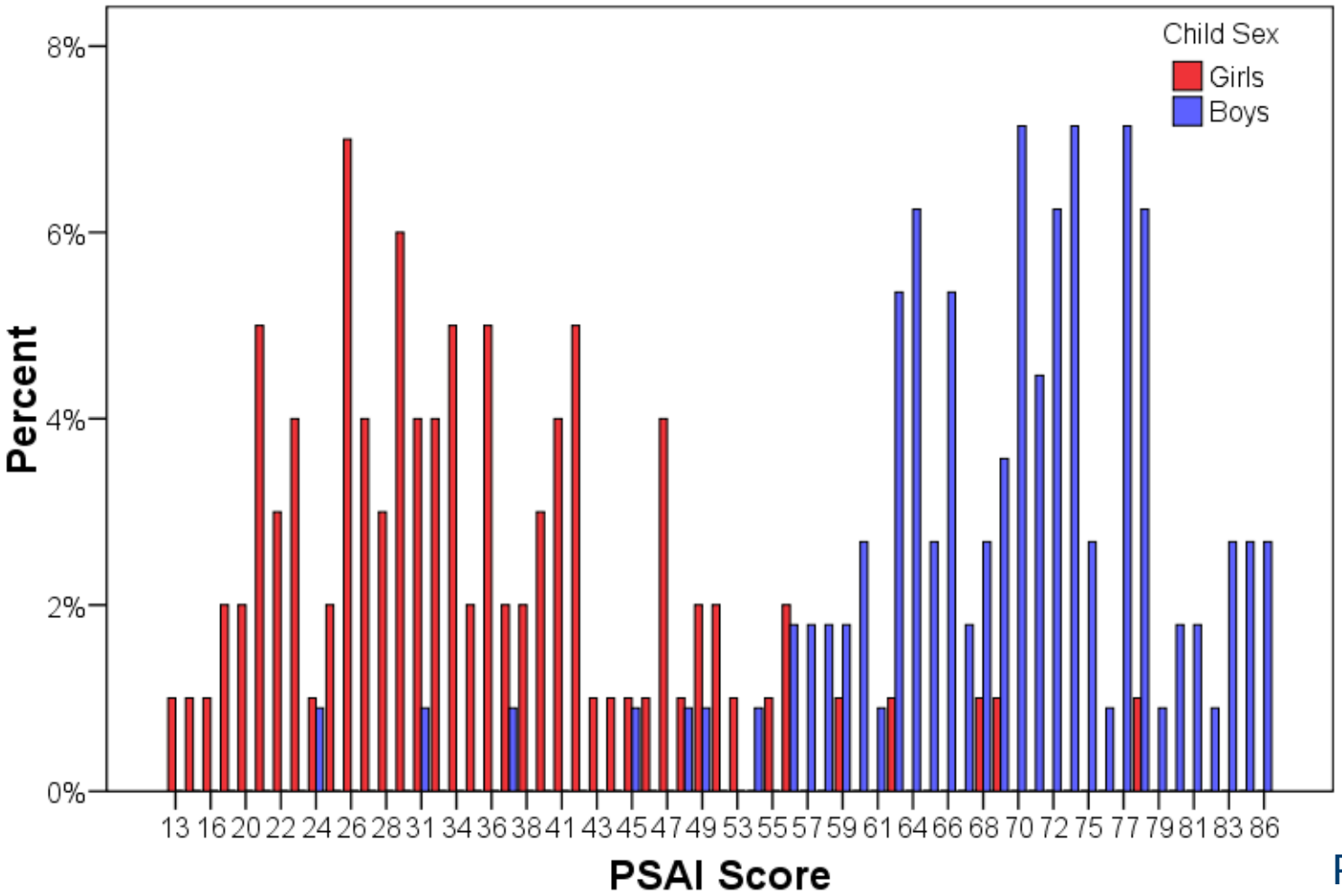
- Animal studies demonstrate hormone effects
- Boys and girls prefer different types of toys
- Boys engage in more rough-and-tumble play
- Boys and girls prefer same sex playmates
- Masculinised behaviour in girls exposed to high androgen levels

fT and Gender-Typical Play

- Pre-School Activities Inventory (Golombok & Rust, 1993)
  - 24 Items (12 Masculine, 12 Feminine)

	Never	Hardly Ever	Some-times	Often	Very Often
Toys					
Guns (or used objects as guns)	1	2	3	4	5
Dolls, doll's clothes or doll's carriage	1	2	3	4	5
Activities					
Playing house (e.g. cleaning, cooking)	1	2	3	4	5
Climbing (e.g. fences, trees, gym equipment)	1	2	3	4	5
Characteristics					
Enjoys rough-and-tumble play	1	2	3	4	5
Avoids getting dirty	1	2	3	4	5

PSAI Scores

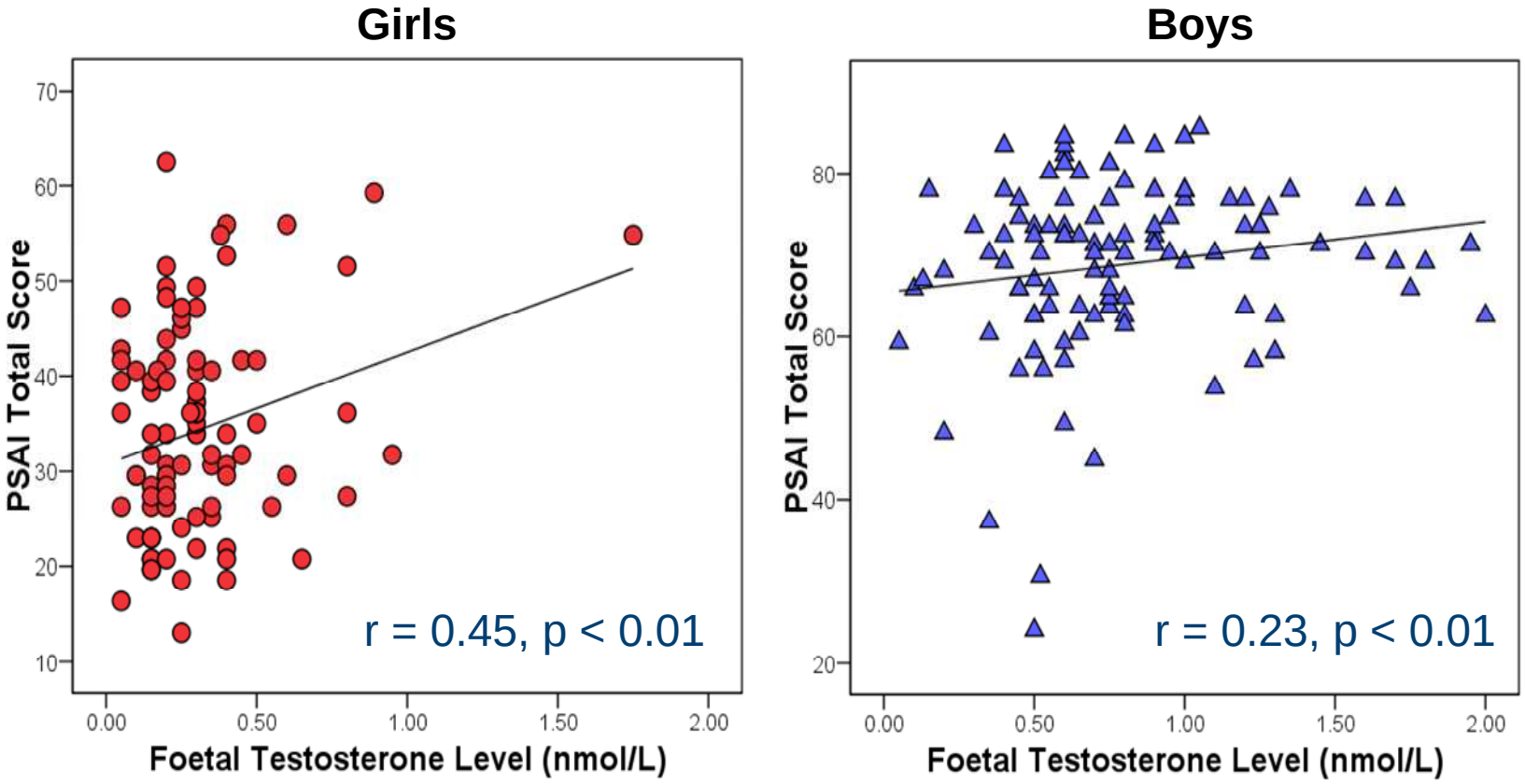


boys n=112	68.9 (11.1)
girls n=100	35.2 (13.0)

Psychol Sci., 2009

fT levels and PSAI scores by sex

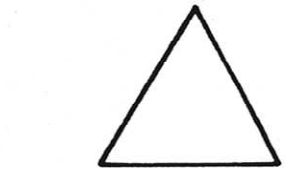
- fT levels and PSAI scores by sex

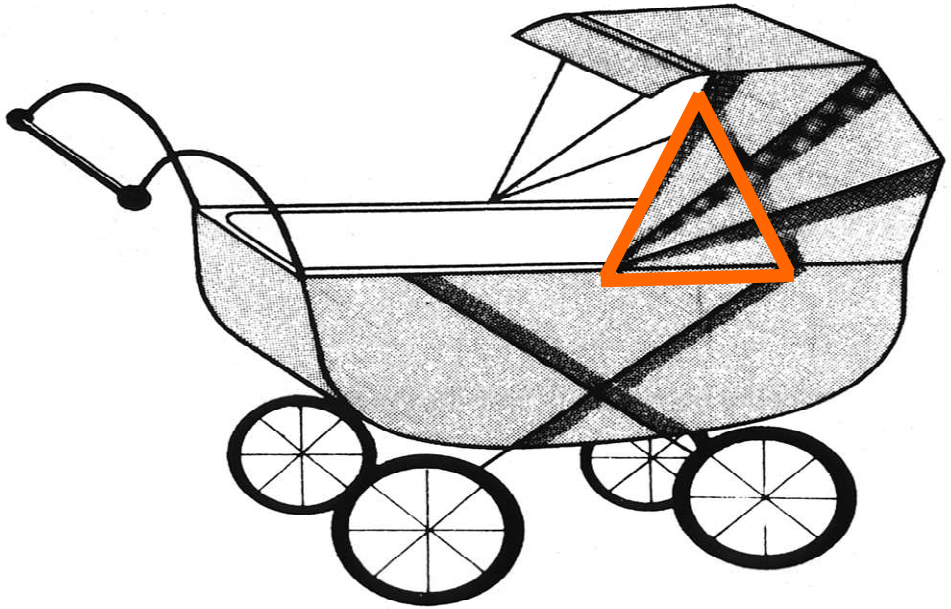


Psychol Sci., 2009

Embedded Figures

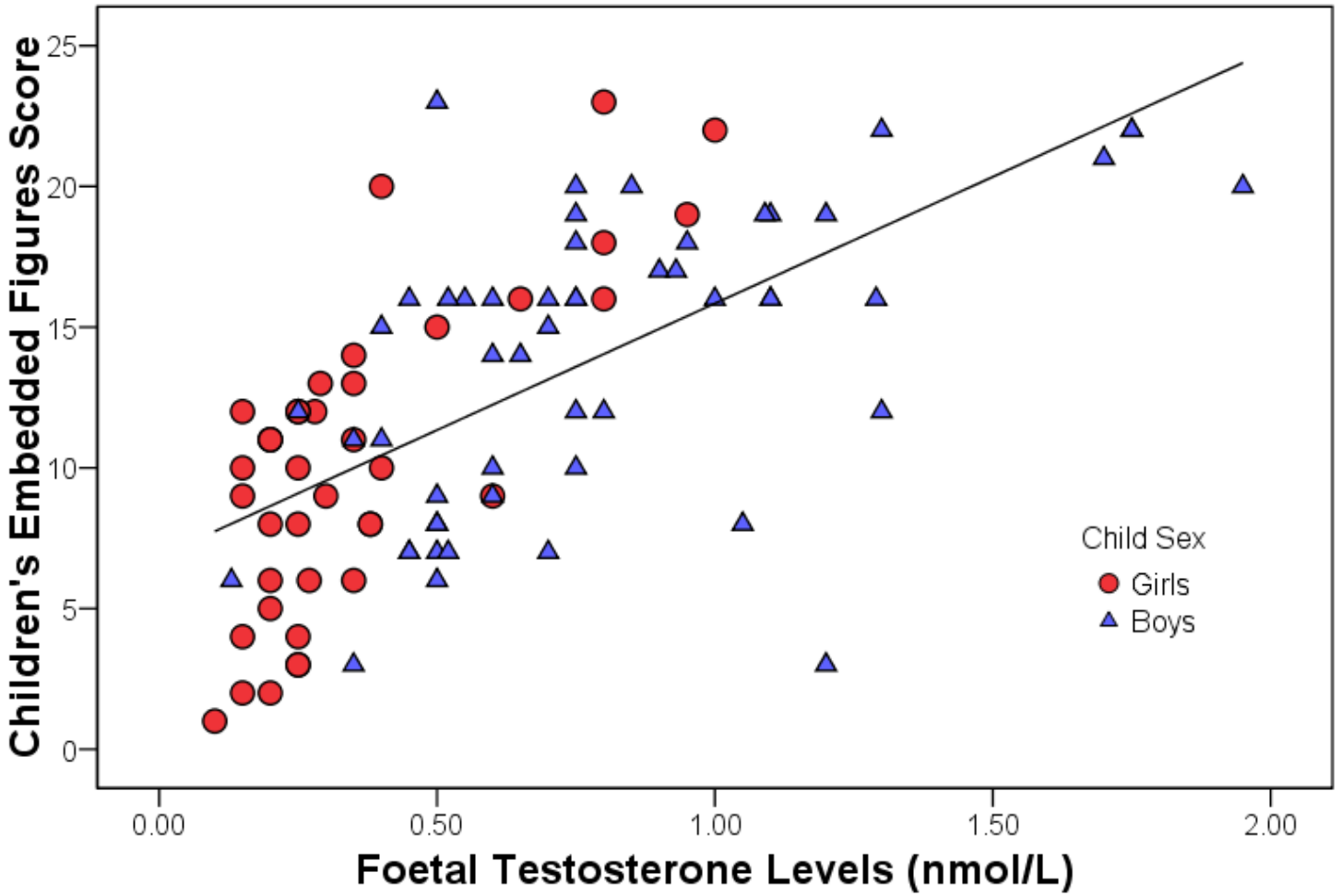
Hidden ‘tent’ figure





(Witkin et al., 1971)

fT and Embedded Figures



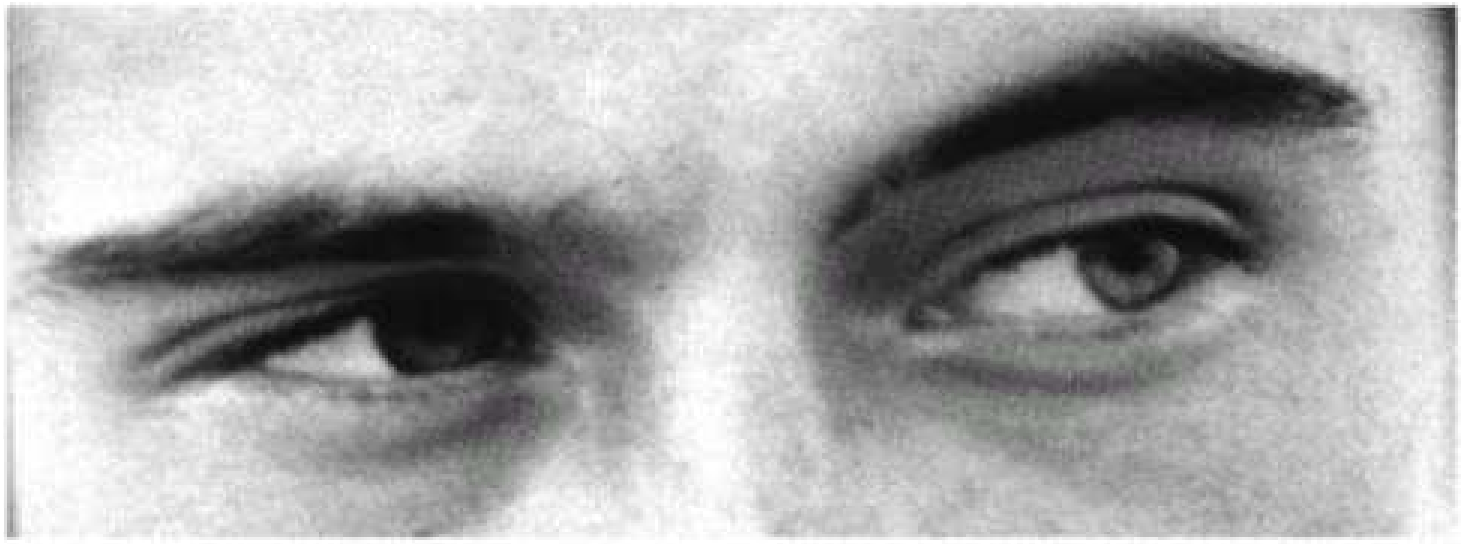
boys n=42	13.7 (5.2)
girls n=56	10.5 (5.12)

$r = 0.57$, $p < 0.01$

Reading the Mind in the Eyes

feeling sorry

bored

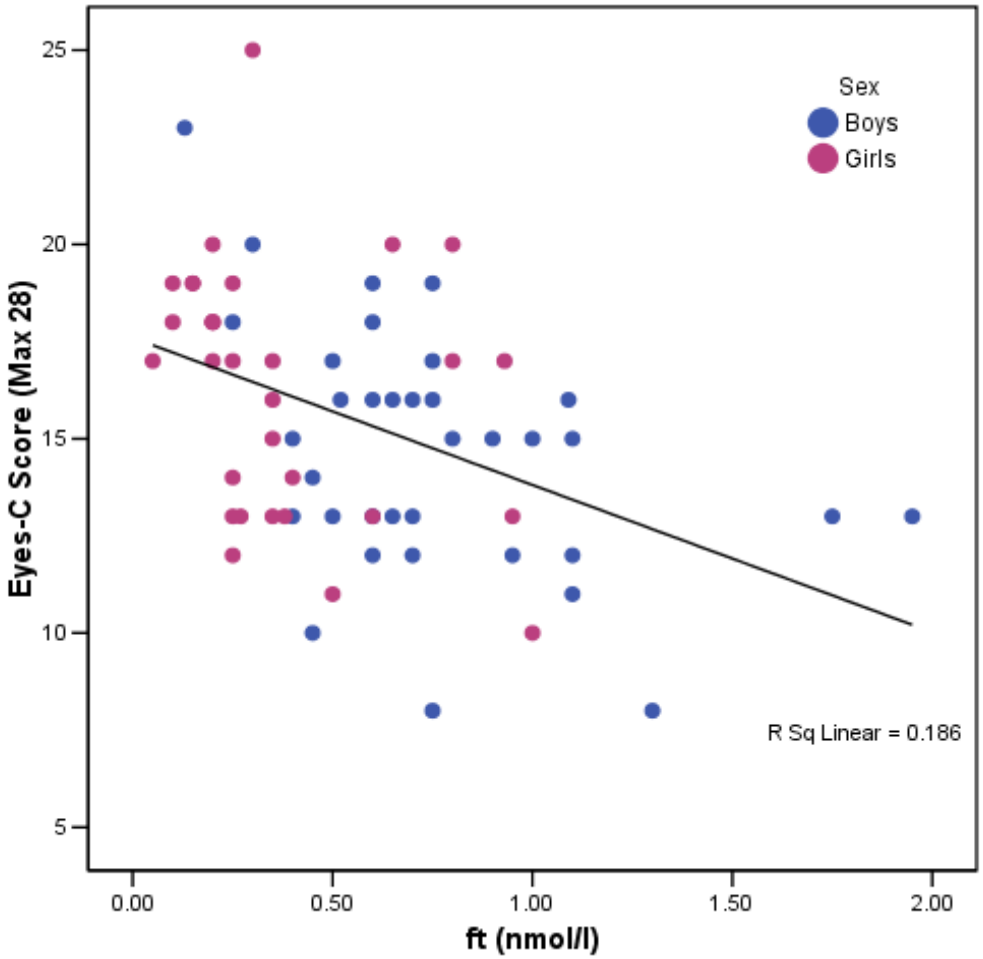


interested

joking

(Baron-Cohen et al., 2001)

fT and Reading the Mind in the Eyes

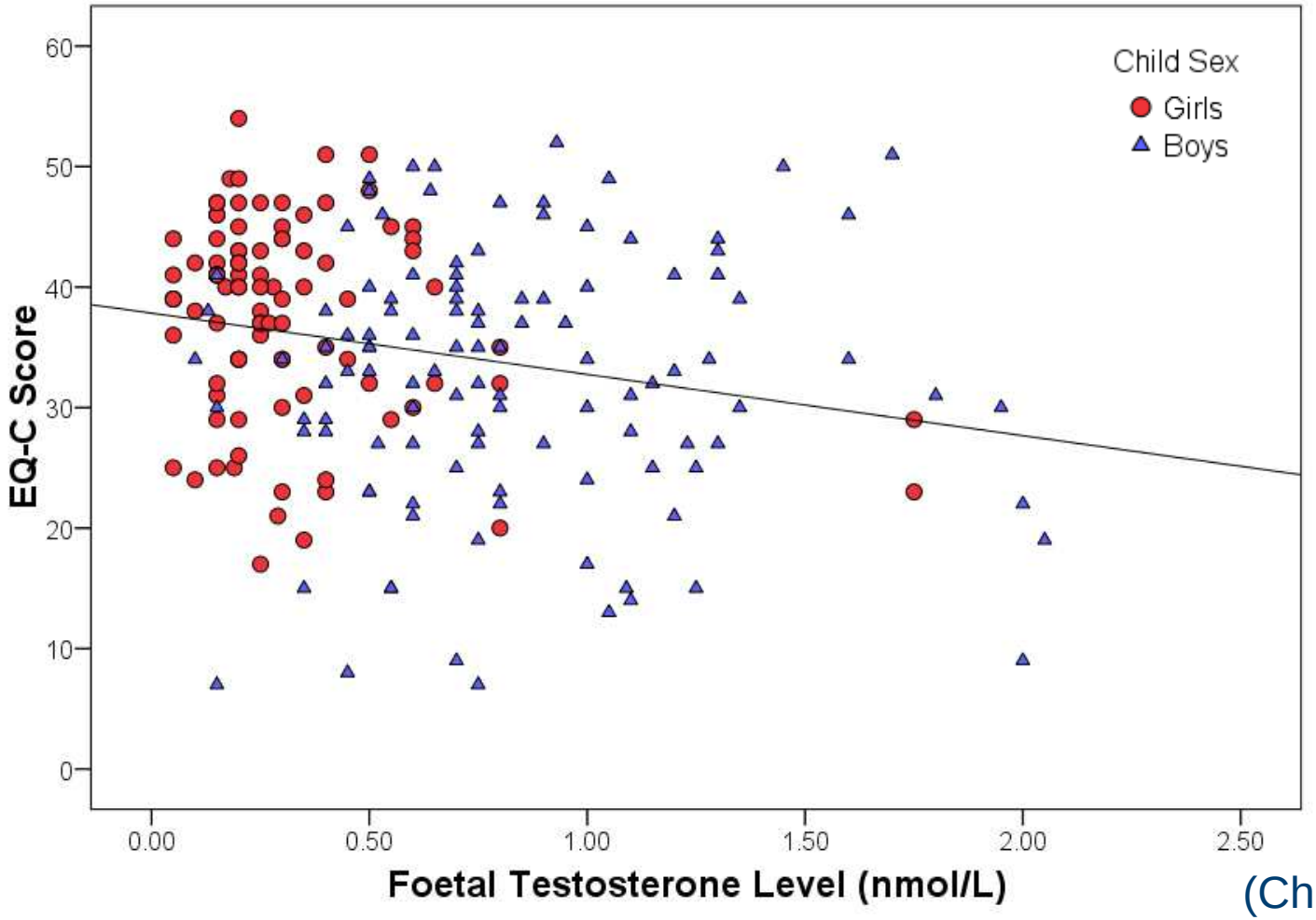


boys n=42	15.2 (3.5)
girls n=56	16.6 (3.3)

$r = -0.43$, $p < 0.01$

(Chapman et al., 2006)

fT and EQ-C Scores

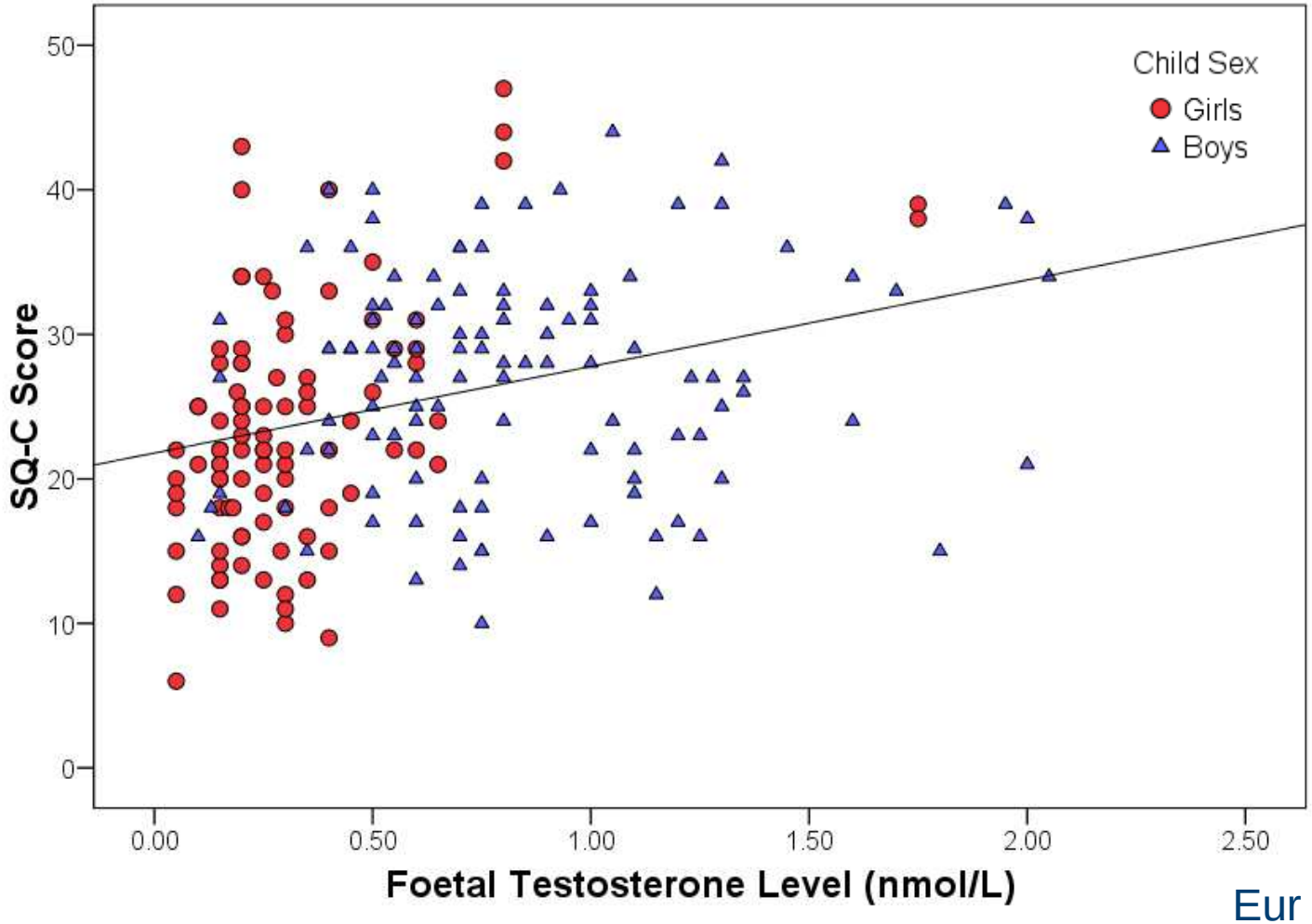


boys n=100	32.6 (9.6)
girls n=93	39.1 (7.4)

$r = -0.28$, $p < 0.01$

(Chapman et al., 2006)

fT and SQ-C Scores

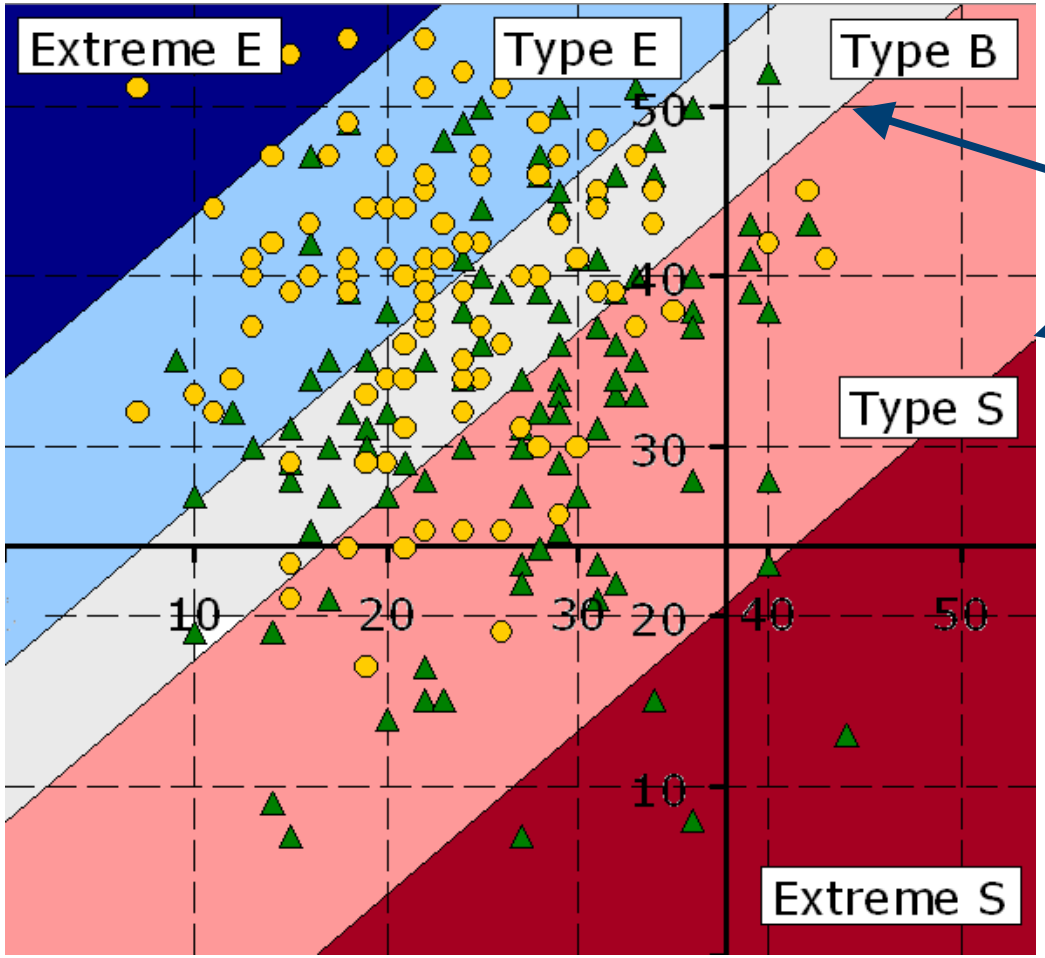


boys n=100	32.6 (9.6)
girls n=93	39.1 (7.4)

$r = 0.38$, $p < 0.01$

Eur J Endocrinol, 2006

Brain Type Distribution

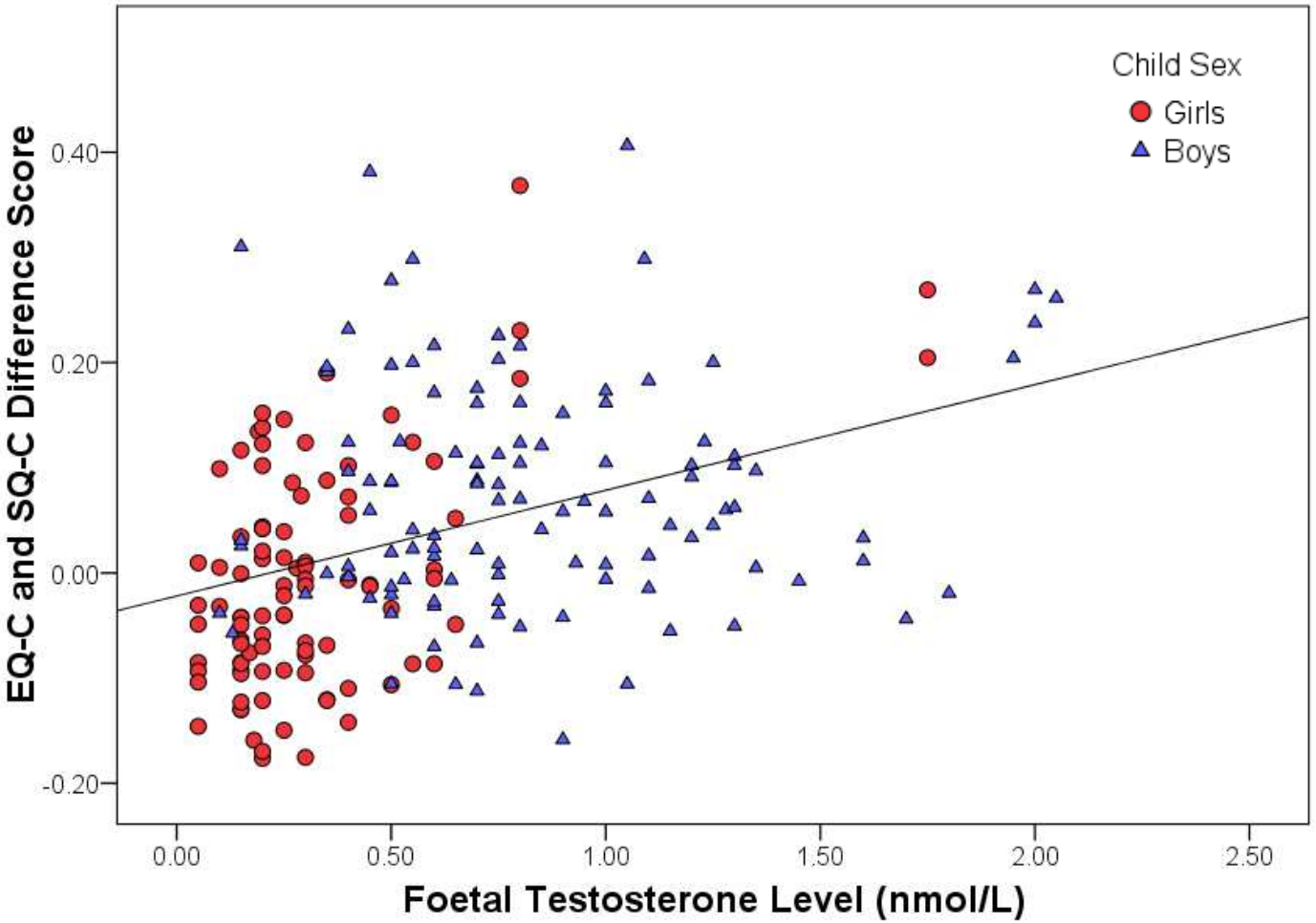


*Boundaries calculated using data from 1250 typically developing children

Boys

Girls

fT and Brain Types



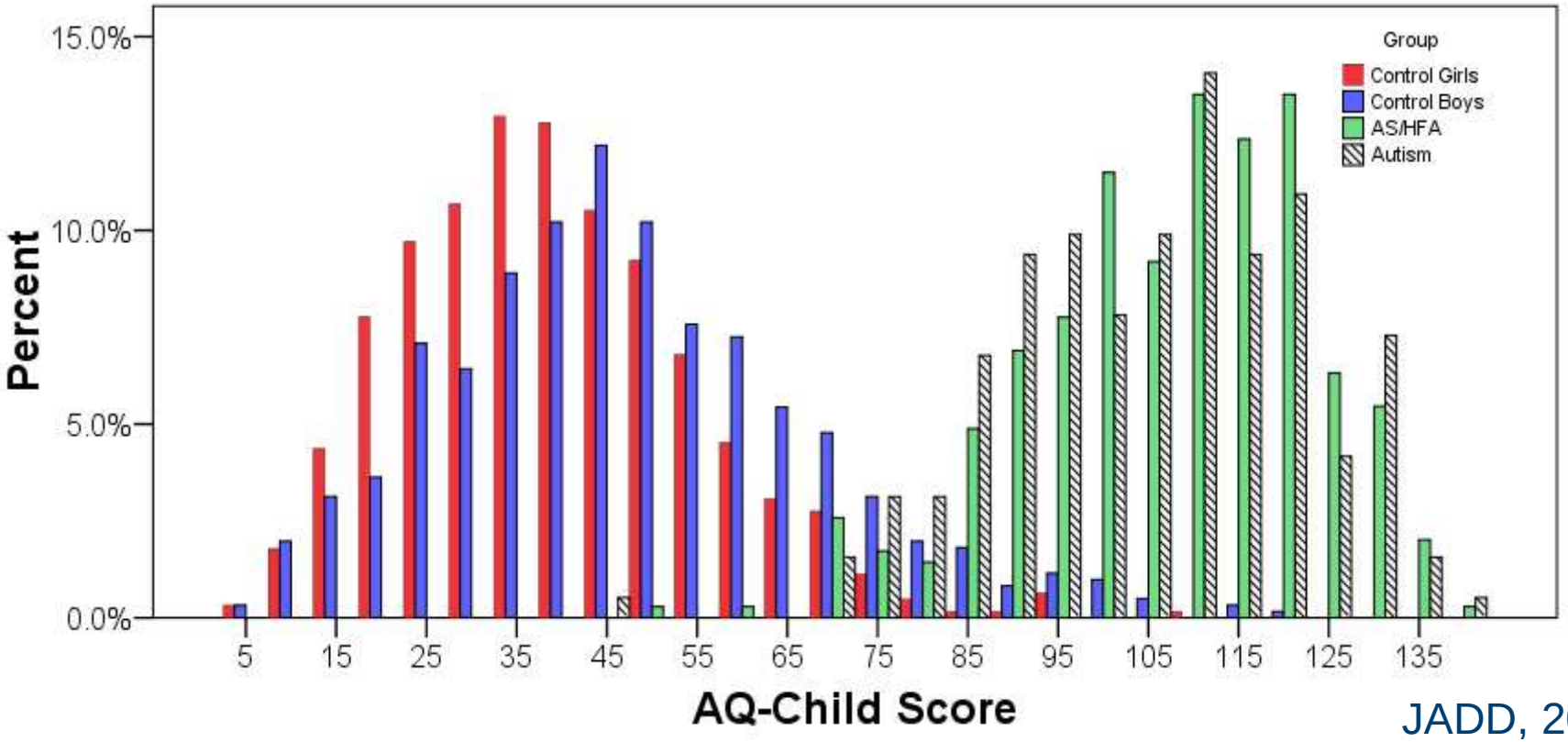
$r = 0.36, p < 0.01$

Measuring Autistic Traits: Autism Spectrum Quotient (AQ)

- Adult and Children's version (AQ-Child)
- 50-item questionnaire
  - I prefer to do things with others rather than on my own
  - I often notice small sounds when others do not
  - S/he prefers to do things with others rather than on her/his own
  - New situations make him/her anxious

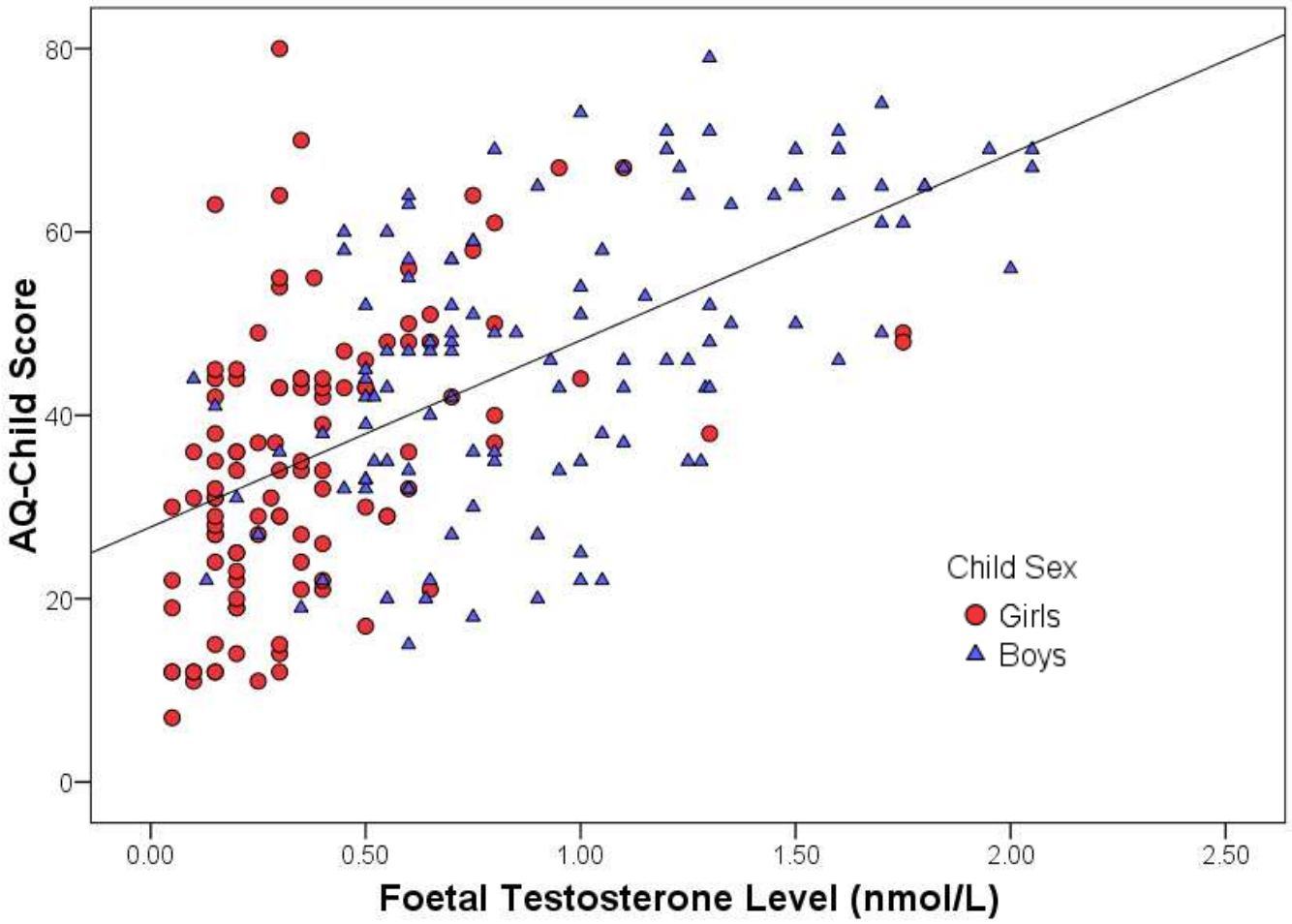
The AQ-Child

- 540 children with ASC, 1225 with no diagnosis
- 4 to 11 years old (M=7.95, SD=1.76)



JADD, 2008

fT and AQ-Child



boys n=124	48.8 (18.0)
girls n=112	34.4 (15.0)

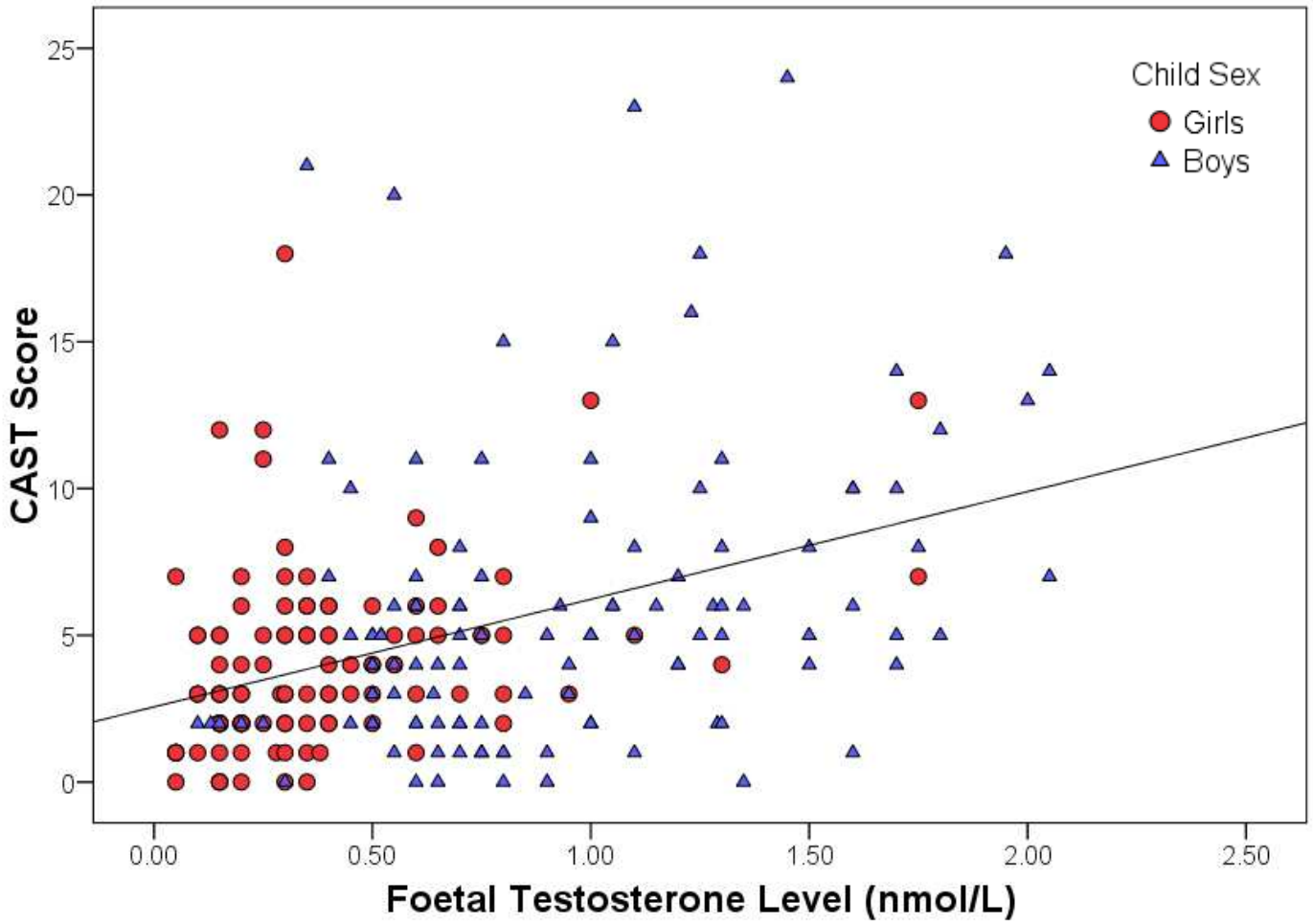
$r = 0.41$, $p < 0.01$

BJP, 2009

Measuring Autistic Traits: the CAST

- Childhood Autism Spectrum Test (CAST)
- 37-item parent-report questionnaire answered in yes/no format
  - Does s/he come up to you spontaneously for a chat?
  - Does s/he appear to notice unusual details that others miss?
  - Does s/he like to do things over and over again, in the same way all the time?

fT and CAST



boys n=124	5.2 (4.4)
girls n=112	4.1 (3.2)

$r = 0.25$, $p < 0.01$

BJP, 2009

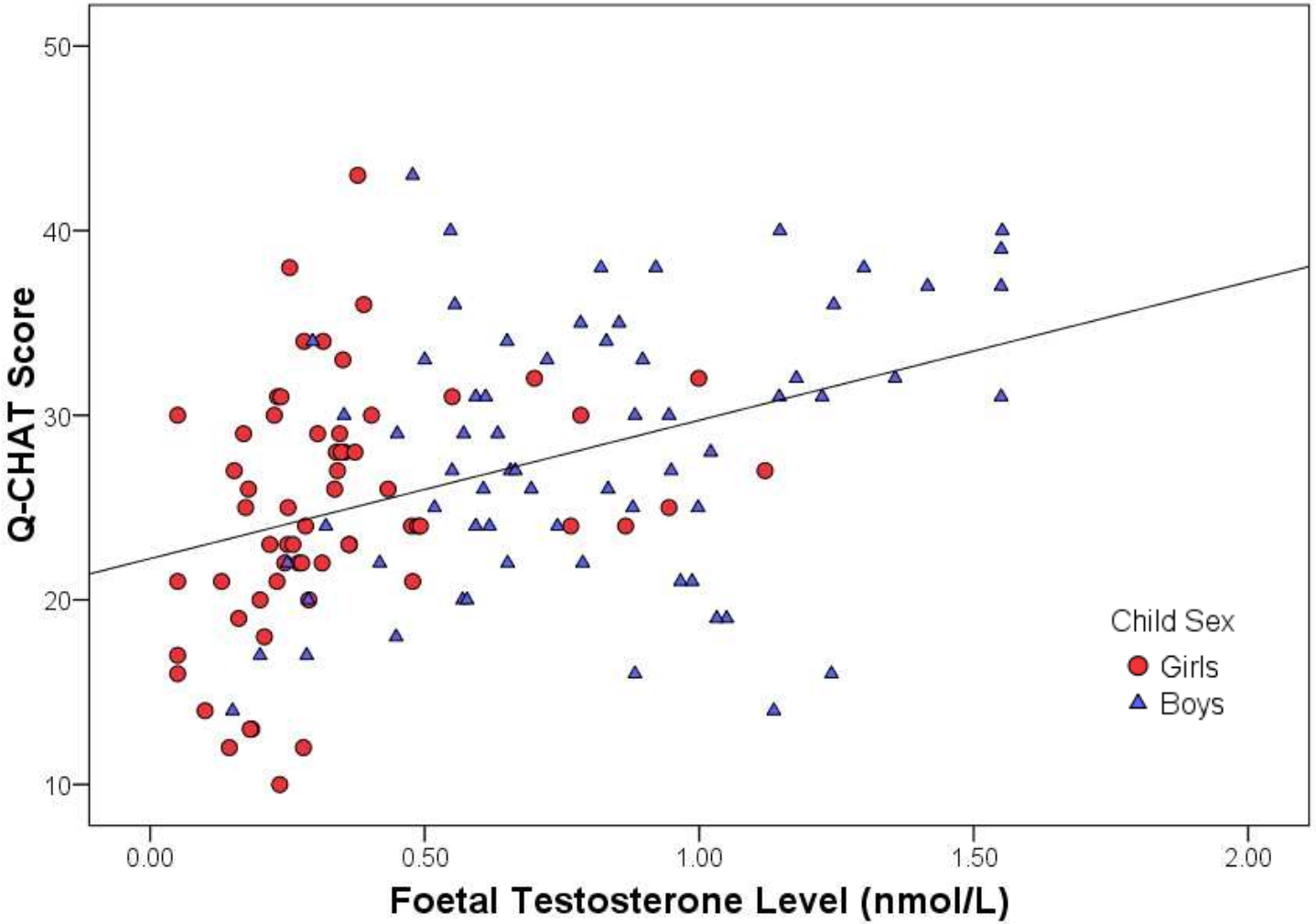
The Quantitative Checklist for Autism in Toddlers (Q-CHAT)

- 26 item parent-report questionnaire (at 18-24 months old)
- Does your child point to share interest with you (e.g. pointing at an interesting sight)?
  - many times a day
  - a few times a day
  - a few times a week
  - less than once a week
  - never

- How easy is it for you to get eye contact with your child?
  - very easy
  - quite easy
  - quite difficult
  - very difficult
  - impossible

(Allison et al., 2008)

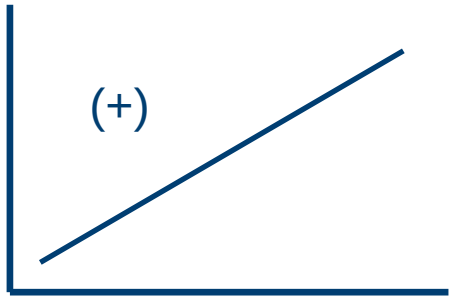
fT and Q-CHAT

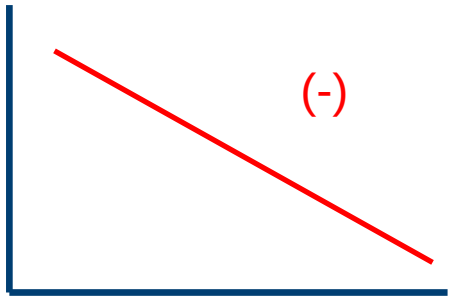


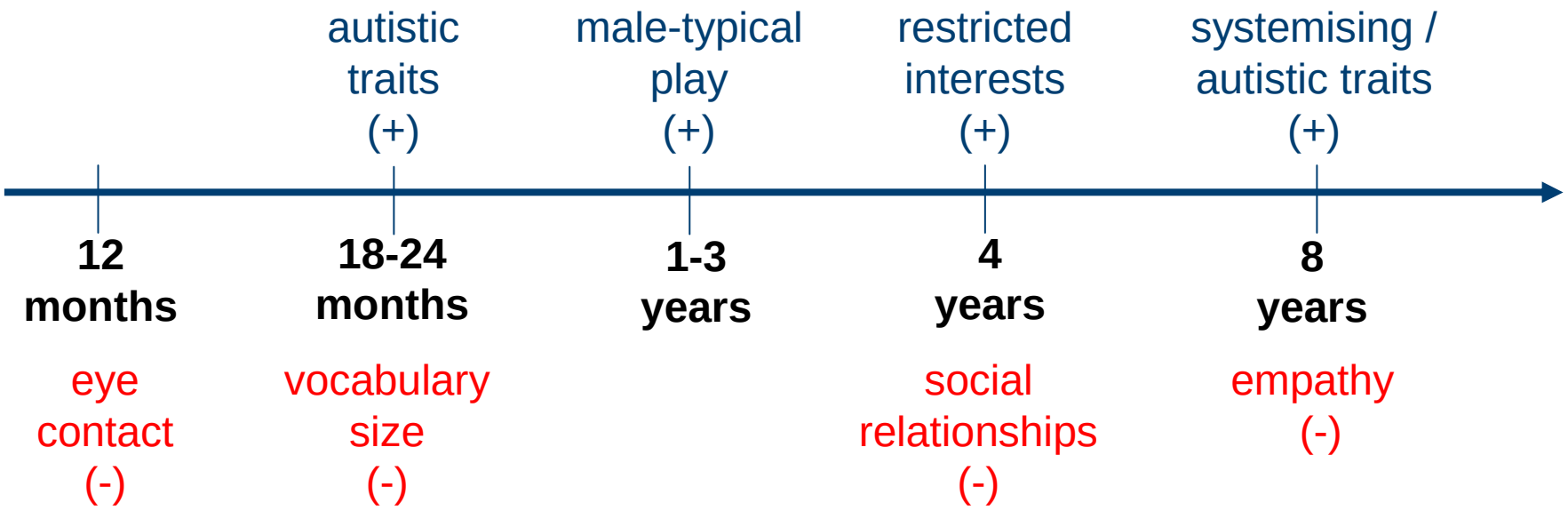
boys n=66	28.1 (6.5)
girls n=63	24.9 (6.5)

$r = 0.40$, $p < 0.01$

Foetal Testosterone and Individual Behaviours







Limitations

- Direct fT measurements from the foetus are not possible
- Single measurement
- No children had a clinical ASC diagnosis
- Effect of postnatal testosterone
- Effects of social factors difficult to quantify
- Parent report

Conclusions

- Sex typical behaviours are found throughout life and may be present as early as the first day of life
- ASC are early onset conditions and have been linked to sex typical behaviours
- Sex typical behaviours have also been found in non-human mammals, suggesting the possibility of a biological component in their development
- Hormones (particularly androgens) are known to have a role in physical and behavioural development
- Research has highlighted a role for fT in the development of sex typical behaviours and the development of Autistic behaviours
- Future work
  - Understand variations in fT between individuals
  - Identify other factors which vary between males, females and individuals with ASC

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